

# PATENT COOPERATION TREATY

**PCT**

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 13 April 2000 (13.04.00)	
<b>International application No.</b> PCT/US99/20957	<b>Applicant's or agent's file reference</b> P50836
<b>International filing date</b> (day/month/year) 15 September 1999 (15.09.99)	<b>Priority date</b> (day/month/year) 18 September 1998 (18.09.98)
<b>Applicant</b> WHITE, John, R.	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
01 March 2000 (01.03.00)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	<b>Authorized officer</b> Pascal Piriou Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

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REC'D 16 JAN 2001

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P50836	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/20957	International filing date (day/month/year) 15 SEPTEMBER 1999	Priority date (day/month/year) 18 SEPTEMBER 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/17 and US Cl.: 514/588, 595, 596, 597, 598		
Applicant SMITHKLINE BEECHAM CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 01 MARCH 2000	Date of completion of this report 30 DECEMBER 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer <b>DELLA MAE COLLINS</b> PARALEGAL SPECIALIST Cybille Delacroix TECHNOLOGY CENTER 1000 Telephone No. (703) 308-0196

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/20957

**I. Basis of the report**1. With regard to the **elements** of the international application:\*☒ the international application as originally filed☒ the description:

pages 1-6 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the claims:

pages 7 , as originally filed  
pages NONE , as amended (together with any statement) under Article 19  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the drawings:

pages 1-4 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the sequence listing part of the description:

pages NONE , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:☐ contained in the international application in printed form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☒ The amendments have resulted in the cancellation of:☒ the description, pages none☒ the claims, Nos. none☒ the drawings, sheets/fig none5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/20957

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. statement

Novelty (N)

Claims	<u>1-6</u>	YES
Claims	<u>none</u>	NO

Inventive Step (IS)

Claims	<u>none</u>	YES
Claims	<u>1-6</u>	NO

Industrial Applicability (IA)

Claims	<u>1-6</u>	YES
Claims	<u>none</u>	NO

## 2. citations and explanations (Rule 70.7)

Claims 1-6 lack an inventive step under PCT Article 33(3) as being obvious over WHITE et al. in view WIDDOWSON.

WHITE et al. disclose methods of administering the CXCR2 antagonist (N-(2-hydroxy-4-nitrophenyl)-N-(2-bromophenyl)urea) to rabbits. Results demonstrate that said antagonist inhibited IL-8 induced neutrophil migration. Please see the abstract.

WHITE does not disclose administration of said CXCR2 antagonists to humans or that said antagonist inhibit T-cell chemotaxis. However, the Examiner refers to WIDDOWSON which discloses that CXCR2 compounds inhibit chemotaxis of neutrophils and T-cells and further that said compounds may be useful in treating a variety of diseases such as psoriasis or asthma. Please see the abstract.

It would have been obvious to one of ordinary skill in the art to modify the method of WHITE to administer the antagonists to humans, as taught by WIDDOWSON, because WIDDOWSON raises reasonable expectation of success by disclosing that CXCR2 compounds are effective in inhibiting neutrophil and T-cell chemotaxis in humans.

----- NEW CITATIONS -----  
NONE



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>A61K 31/17</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 00/16768</b> <b>(43) International Publication Date:</b> 30 March 2000 (30.03.00)
<b>(21) International Application Number:</b> PCT/US99/20957 <b>(22) International Filing Date:</b> 15 September 1999 (15.09.99) <b>(30) Priority Data:</b> 60/101,021 18 September 1998 (18.09.98) US <b>(71) Applicant (for all designated States except US):</b> SMITHKLINE BEECHAM CORPORATION [US/US]; One Franklin Plaza, Philadelphia, PA 19103 (US). <b>(72) Inventor; and</b> <b>(75) Inventor/Applicant (for US only):</b> WHITE, John, R. [GB/US]; 332 Jennifer Drive, Coatesville, PA 19320 (US). <b>(74) Agents:</b> SIMON, Soma, G. et al.; SmithKline Beecham Corporation, Corporate Intellectual Property, UW2220, 709 Swedeland Road, P.O. Box 1539, King of Prussia, PA 19406-0939 (US).		<b>(81) Designated States:</b> AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> CXCR2 INHIBITORS AND PMN ADHESION AND T-CELL CHEMOTAXIS		
<b>(57) Abstract</b>  The present invention is a method of inhibiting, or blocking, the binding of human neutrophils to activated endothelial cells, or T-cell mediated chemotaxis in a patient in need thereof, which method comprises administering to said patient an effective amount of a compound which binds the CXCR2 receptor.		

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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/20957**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) :A61K 31/17

US CL :514/588, 595, 596, 597, 598

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/588, 595, 596, 597, 598

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN, REG, CAPLUS, BIOSIS, MEDLINE, USPATFULL

CXCR2, CXCR1 receptors, inhibitors, inflammation, arthritis, reperfusion, atherosclerosis, astham, chemtoaxis, chemokines

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WHITE et al. Identification of a Potent, Selective Non-peptide CXCR2 Antagonist That Inhibits Interleukin-8-induced Neutrophil Migration. J. Biol. Chem. 24 April 1998, Vol. 273. Issue 17, pages 10095-10098, see entire document.	1-6
Y	Database DERWENT, DERWENT INFORMATION LTD, Acc. No. 1998-110158, WIDDOWSON, K.L. 'N- ((2-Acidic substituted) aza-aryl) -N'-arylalkyl urea(s) and thiourea(s) - which bind to IL-8 receptors are used for treating psoriasis, arthritis, asthma, ARDS, IBD, stroke, shock, thrombosis or Alzheimer's disease,' abstract, WO 9749400 A1, 31 December 1997 (31/12/97).	1-6

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

06 NOVEMBER 1999

Date of mailing of the international search report

20 JAN 2000

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